IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
NAKAI et al.	Art Unit: 1633
Application No.: 09/897,988	Examiner: Maria Marvich
Filing Date: July 5, 2001	Attorney Ref. No.: US-142O
For: METHOD FOR PRODUCING SUBSTANCE UTILIZING MICROORGANISM	Confirmation No.: 1677

BRIEF FOR APPELLANT

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

COMES NOW the Appellant to present this Brief in support of the appeal of the final rejections of Claims 1, 7, and 12-14 in the above-captioned patent application. The Notice of Appeal having been timely filed on 17 October 2006, this Brief is due to be filed on 17 December 2006.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. If, however, additional extensions of time are necessary to prevent abandonment of this application or dismissal of this appeal, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is hereby authorized to charge fees necessitated by this paper, and to credit all refunds and overpayments, to the credit card utilized in EFS-Web processing.

For the following reasons, Appellant respectfully submits that the final rejection of each of Claims 1, 7, and 12-14 in this application is in error, and therefore respectfully requests reversal of the rejections.

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I. Real Party in Interest

The real party in interest is Ajinomoto Co., Inc, a corporation of Japan.

II. Related Appeals and Interferences

There are no related appeals or interferences.

III. Status of Claims

Claims 1, 6, 7, and 11-14 are pending. No claims are in condition for allowance. Claims 6 and 11 are objected to by the Examiner, but would be allowable if they were made independent. Claims 1, 7, and 12-14 stand finally rejected in the Office Action dated 28 July 2006, and are on appeal. Claims 2-5 and 8-10 have been cancelled.

IV. Status of Amendments

All amendments to the claims have been entered.

V. Summary of the Claimed Subject Matter

The present invention relates to a method for producing a target substance comprising culturing an *Escherichia coli* strain in a medium; and collecting said substance from said medium, wherein the *Escherichia coli* strain has an ability to produce and accumulate the target substance in the medium and has been modified so to have a characteristic selected from the group consisting of: i) enhanced activity of an enzyme selected from the group consisting of

cytochrome bo-type oxidase and NDH-1, wherein said activity is enhanced by increasing a copy number of a gene coding for said enzyme or by modifying an expression regulatory sequence of said gene, and/or (ii) deficient activity of an enzyme selected from the group consisting of cytochrome bd type oxidase and NDH-II, wherein said activity is made deficient by disrupting a gene coding for said enzyme, wherein the target substance is selected from the group consisting of an L-amino acid, specifically L-lysine, L-threonine, or L-phenylalanine, and a nucleic acid (see the specification at page 8, line 25 through page 18, line 25). The present invention also relates to the method as described above, wherein said strain comprises enhanced cytochrome bo-type oxidase activity and deficient NDH-II activity (see the specification at page 11, line 9 through page 18, line 25.

VI. Grounds of Rejection to Be Reviewed on Appeal

A. Whether claims 1, 7, and 12-14 are anticipated under 35 U.S.C. §102(b) over Ciccognani et al. (FEMS Microbiology Letters 94, 1992, 1-6).

B. Whether clams 1, 7, and 12-14 are anticipated under 35 U.S.C. §102(a) over Spehr et al. (Biochemistry, 1999, vol. 38, 16261-16267).

VII. Argument

A. Introduction

In the Office Action dated July 28, 2006 ("Final Office Action"), beginning at page 2, Claims 1, 7, and 12-14 were rejected under 35 U.S.C. § 102(b), as reciting subject matters that

allegedly are anticipated by Ciccognani *et al.*. Also, beginning at page 3, Claims 1, 7, and 12-14 were rejected under 35 U.S.C. § 102(a), as reciting subject matters that allegedly are anticipated by Spehr *et al.*.

For at least the following reasons, these rejections are in error and should be reversed.

B. Legal Standard

Claim construction begins with the words of the claims. *Karlin Tech., Inc. v. Surgical Dynamics, Inc.*, 177 F.3d 968, 971 (Fed. Cir. 1999). Claim language should be interpreted as one reasonably skilled in the art would have interpreted the claim at the time of the patent application date. *Vivid Techs., Inc. v. American Science & Engineering, Inc.*, 200 F.3d 795, 804 (Fed. Cir. 1999); *Wiener v. NEC Elec., Inc.*, 102 F.3d 534, 539 (Fed. Cir. 1996). Where the claim term has no specialized meaning to persons of skill in the art, the ordinary meaning of the words to those of ordinary skill in the art controls, unless the evidence indicates that the inventor used them differently. *Karlin*, 177 F.3d at 971. Such evidence includes the specification and prosecution history, both of which must be analyzed to determine if the inventor limited or redefined any of those terms. *Watts v. XL Sys., Inc.*, 232 F.3d 877, 882-84 (Fed. Cir. 2000); *Vivid Techs.*, 200 F.3d at 804. If claim language is not clear on its face, then intrinsic evidence also should be consulted to resolve the lack of clarity. *Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001).

Under the doctrine of anticipation, a patent claim is not patentable if the claimed invention lacks novelty. 35 U.S.C. § 102(b); *Karsten Mfg. Comp v. Cleveland Golf*, 242 F.3d

1376, 1383 (Fed. Cir. 2001). Anticipation, a question of fact, focuses on a comparison of the prior art to the subject matter of the claim at issue. *Celeritas Technologies, Ltd. v. Rockwell International Corp.* 150 F.3d 1354, 1361 (Fed. Cir. 1998). "[A] claim is anticipated if each and every limitation is found either expressly or inherently in a single prior art reference." *Celeritas*, 150 F.3d at 1361. A convenient way to consider anticipation is the "four corners" doctrine. The "four corners" doctrine refers to the idea that anticipation requires that each and every limitation of the claimed invention is described either expressly or inherently within the four corners of a single prior art document. *Advanced Display Systems, Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000).

To anticipate, the prior art reference must also enable one of ordinary skill in the art to make and use the claimed invention, *i.e.*, must be enabling. *Transclean Corp. v. Bridgewood Service, Inc.*, 290 F.3d 1364 (Fed. Cir. 2002) (*citing In re Donohue*, 766 F.2d 531, 533 (Fed. Cir. 1985)). The test for a non-enabling disclosure is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art, without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988). As the Court of Appeals for the Federal Circuit explained in *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003), "a non-enabled disclosure cannot be anticipatory (because it is not truly prior art) if that disclosure fails to enable one of skill in the art to reduce the disclosed invention to practice."

C. The rejection of Claims 1, 7, and 12-14 under 35 U.S.C. §102(b) is in error

In the Office Action, beginning at page 16, Claims 1-3, 7 and 10 were rejected under 35 U.S.C. § 102(b), as reciting subject matters that allegedly are anticipated by Ciccognani *et al.* Applicants respectfully request reconsideration of this rejection.

The claims recite a method for producing an L-amino acid or a nucleic acid in an *Escherichia coli* culture in medium, wherein the bacterium has been modified to have an enhanced activity of either cytochrome bo-type oxidase or NDH-I, and to be deficient in the activity of cytochrome bd type oxidase or NDH-II. Finally, the produced L-amino acid and/or nucleic acid is collected from the medium. The claims explicitly require that the produced target substance, the L-amino acid and/or nucleic acid, is collected from the medium in which the *E. coli* is cultured, and that the *E. coli* has the ability to produce and accumulate the target substance in the medium.

Ciccognani *et al.* fails to anticipate the claimed invention since it does not explicitly or inherently teach each and every limitation of the claimed invention. Specifically, no method is taught by which a target substance is produced. Even more specifically, since no such method is taught, there can be no teaching or suggestion of any sort of collection of a target substance, as recited in step B) of the claimed method.

Although the Final Office Action asserts that there is no explicit or inherent requirement that the claimed strain excrete the target substances, this assertion actually has no bearing on whether the Ciccognani *et al.* teaches the step of "collecting the target substance". Specifically,

the claims recite that the target substance is ***collected*** from the medium in which the cells are cultured, and further that the cells have an ability to produce and accumulate said target substance in the medium. The Office Action has stated that the presence of the target substance within the cell still falls within "in the medium", since the cell is in the medium. While such a construction might be possible, this claim construction still does not alleviate the problem or issue that Ciccognani *et al.* does not teach ***collection*** of the target substance from the medium, whether from within the cell, or as an excretion product of the cell. Such positive methods steps clearly distinguish the claims over the teachings of Ciccognani *et al.*, which clearly does not teach or suggest any excretion of any target substance into the medium, let alone the collection of any such substance. Therefore Ciccognani *et al.* fails to satisfy the "four corners" doctrine, in that not every limitation of the claims is recited in the single prior art reference. *Advanced Display Systems, Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000).

Finally, the strain used in the claimed method has an inherent ability to produce and accumulate target substances in the medium when such a strain is cultured in the medium, and this ability is not inherently or explicitly taught or suggested by the cited prior art. The phrase "ability to produce and accumulate the target substance" means an ability to produce L-amino acid and nucleic acid in an amount more than the amount required for growth of the bacterium, that is, an ability to overproduce L-amino acid and nucleic acid, and therefore, the overproduced L-amino acid and nucleic acid are secreted to the culture medium and collected from the medium. Ciccognani *et al.* fail to teach any type of method using such a strain. Such a distinguishing characteristic, combined with the failure to teach the collection step, are sufficient

to remove the cited prior art references, and as such, the claims are not unpatentable under 35 U.S.C. § 102. Therefore, Applicants respectfully request withdrawal of the rejection thereof under 35 U.S.C. § 102 over the cited prior art.

D. The rejection of Claims 1, 7 and 12-14 under 35 U.S.C. §102(a) is in error

In the Office Action, beginning at page 17, Claims 1, 2, 7 and 10 were rejected under 35 U.S.C. § 102(a), as reciting subject matters that allegedly are anticipated by Spehr *et al.* Applicants respectfully request reconsideration of this rejection.

Similar to the above rejection over Ciccognani *et al.,* Spehr *et al.* fail to teach a method of producing and collecting a target substance, such as an L-amino acid or nucleic acid. More importantly, however, Spehr *et al.* fail to teach the characteristic of the strain that it be deficient in an activity of an enzyme such as cytochrome bd type oxidase and/or NDH-II. Therefore, Spehr *et al.* also do not teach each and every aspect of the claimed invention.

The method of the claimed invention recites that the produced target substance is collected from the medium in which the *E. coli* is cultured, and that the *E. coli* has the ability to produce and accumulate the target substance in the medium in which it is cultured. Similar to above, the strain taught by Spehr *et al.* does not produce and accumulate the target substance in the culture medium, whether within the medium inside or outside of the cell walls, and therefore, the target substance cannot be collected from the medium. This aspect of the method is not taught, either explicitly or inherently, by Spehr *et al.*. For these reasons, the claims are not unpatentable under 35 U.S.C. § 102(a). Therefore, Appellants respectfully request withdrawal of the rejection

thereof under 35 U.S.C. § 102 over the cited prior art.

IX. Conclusion

For at least the foregoing reasons, Appellants respectfully submit that the subject matters of Claims 1, 7, and 12-14, each taken as a whole, are patentable. Accordingly, Appellant respectfully requests reversal of the rejections of Claims 1, 7, and 12-14 under sections 102(a) and 102(b).

Respectfully submitted,

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APPENDIX A: CLAIMS ON APPEAL

1. A method for producing a target substance, comprising:

A) culturing an *Escherichia coli* strain in a medium; and

B) collecting said substance from said medium,

wherein the *Escherichia coli* strain has an ability to produce and accumulate the target substance in the medium and has been modified so to have a characteristic selected from the group consisting of:

(i) enhanced activity of an enzyme selected from the group consisting of cytochrome bo-type oxidase and NDH-1, wherein said activity is enhanced by increasing a copy number of a gene coding for said enzyme or by modifying an expression regulatory sequence of said gene,

(ii) deficient activity of an enzyme selected from the group consisting of cytochrome bd type oxidase and NDH-II, wherein said activity is made deficient by disrupting a gene coding for said enzyme, and

(iii) combinations thereof,

wherein the target substance is selected from the group consisting of an L-amino acid and a nucleic acid.

6. The method according to Claim 1, wherein said strain comprises enhanced cytochrome bo-type oxidase activity and deficient NDH-II activity.

7. The method according to Claim 1, wherein said enhanced activity is cytochrome bo-type oxidase activity.

11. The method according to claim 1, wherein said deficient activity is NDH-II activity.

12. The method according to claim 1, wherein said target substance is L-lysine.

13. The method according to claim 1, wherein said target substance is L-threonine.

14. The method according to claim 1, wherein said target substance is L-phenylalanine.

APPENDIX B: EVIDENCE

None.

APPENDIX C: RELATED PROCEEDINGS

None.